

FILE 'REGISTRY' ENTERED AT 12:30:17 ON 12 JUN 2009

EXP DIOXOLANE THYMINE/CN

STRUCTURE UPLOADED

L1

L2

8 S L1

FILE 'STNGUIDE' ENTERED AT 12:31:38 ON 12 JUN 2009

FILE 'REGISTRY' ENTERED AT 12:32:44 ON 12 JUN 2009

STRUCTURE UPLOADED

L3

L4

L5

1 S L3

70 S L3 SSS FULL

FILE 'HCAPLUS' ENTERED AT 12:33:09 ON 12 JUN 2009

L6

L7

L8

16 S L5/THU

137840 S HIV OR (HUMAN IMMUNODEFICIENCY VIRUS) OR AIDS OR K65R OR M184

14 S L6 AND L7

=> file registry
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.22	0.22

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 12:30:17 ON 12 JUN 2009
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5
DICTIONARY FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

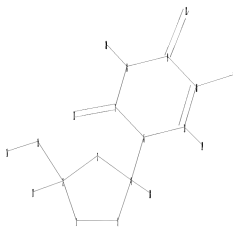
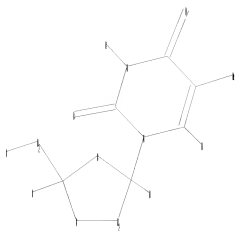
<http://www.cas.org/support/stngen/stdoc/properties.html>

=> exp dioxolane thymine/cn

E1	1	DIOXOLANE POLYMERS/CN
E2	1	DIOXOLANE T/CN
E3	0 -->	DIOXOLANE THYMINE/CN
E4	1	DIOXOLANE-1,2,6-HEXANETRIOL FORMAL-TRIOXANE COPOLYMER/CN
E5	1	DIOXOLANE-1,3,5-TRIOXANE COPOLYMER/CN
E6	1	DIOXOLANE-2,2-BIS(4-GLYCIDYLOXYPHENYL)PROPANE-TRIOXANE COPOLYMER/CN
E7	1	DIOXOLANE-3,4-EPOXY-6-METHYLCYCLOHEXYLMETHYL 3,4-EPOXY-6-METHYLCYCLOHEXANECARBOXYLATE-TRIOXANE COPOLYMER/CN
E8	1	DIOXOLANE-ETHYLENE OXIDE-TETRAHYDROFURAN-TRIOXANE POLYMER/CN
E9	1	DIOXOLANE-ETHYLENE OXIDE-TRIOXANE COPOLYMER/CN
E10	1	DIOXOLANE-FORMALDEHYDE COPOLYMER/CN
E11	1	DIOXOLANE-FORMALDEHYDE POLYMER/CN
E12	1	DIOXOLANE-FORMALDEHYDE-POLYCAPROAMIDE POLYMER/CN

=>

Uploading C:\Program Files\STNEXP\Queries\10530088dioxolane.str



```

chain nodes :
12 13 14 15 16 17 18 19 20
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
2-15 2-17 4-6 4-18 7-13 8-20 9-12 10-14 11-19 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 6-7 6-11 7-8 7-13 8-9 9-10 9-12 10-11
exact bonds :
2-15 2-17 4-18 8-20 10-14 11-19 15-16

```

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS

```

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 12:31:05 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**

PROJECTED ITERATIONS: 22 TO 418

PROJECTED ANSWERS: 8 TO 329

L2 8 SEA SSS SAM L1

=> d l2 scan

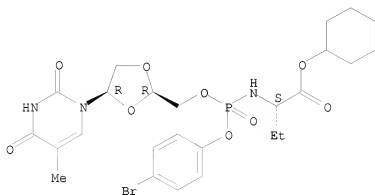
L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN Butanoic acid, 2-[(4-bromophenoxy)][(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-

dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phosphinyl]amino]-,
cyclohexyl ester, (2S)-

MF C25 H33 Br N3 O9 P

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

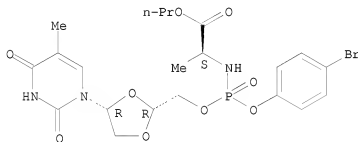
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN L-Alanine, N-[(4-bromophenoxy)[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phosphinyl]-, propyl ester

MF C21 H27 Br N3 O9 P

Absolute stereochemistry.



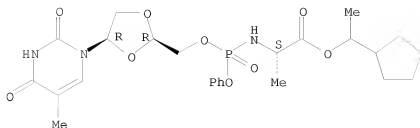
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN

IN L-Alanine, N-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]phenoxyphosphinyl]-, 1-cyclopentylethyl ester

MF C25 H34 N3 O9 P

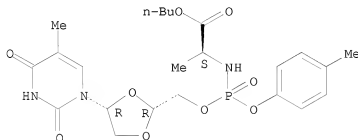
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 8 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
 IN L-Alanine, N-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-
 pyrimidinyl)-1,3-dioxolan-2-yl]methoxy](4-methylphenoxy)phosphinyl]-,
 butyl ester
 MF C23 H32 N3 O9 P

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file stnguide
 COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.96	1.18

FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 12:31:38 ON 12 JUN 2009
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Jun 5, 2009 (20090605/UP).

=>
 Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.14

1.32

FILE 'REGISTRY' ENTERED AT 12:32:44 ON 12 JUN 2009

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5

DICTIONARY FILE UPDATES: 10 JUN 2009 HIGHEST RN 1155458-91-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

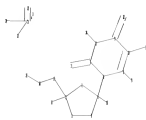
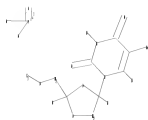
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\STNEXP\Queries\10530088dioxolane2.str



```

chain nodes :
12 13 14 15 16 17 18 19 20 21 22 23 24 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11
chain bonds :
2-15 2-17 4-6 4-18 7-13 8-20 9-12 10-14 11-19 15-16 16-27 21-22 21-23
21-24
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 6-7 6-11 7-8 7-13 8-9 9-10 9-12 10-11 16-27
21-22 21-23 21-24
exact bonds :
2-15 2-17 4-18 8-20 10-14 11-19 15-16

```

G1:C,H,[*1]

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 27:CLASS

```

=> s 13
SAMPLE SEARCH INITIATED 12:32:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

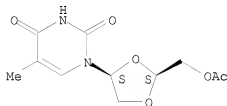
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 22 TO 418
PROJECTED ANSWERS: 1 TO 80

L4 1 SEA SSS SAM L3

=> d 14 scan

L4 1 ANSWERS REGISTRY COPYRIGHT 2009 ACS on STN
IN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-[(acetyloxy)methyl]-1,3-dioxolan-4-yl]-5-methyl-, rel-
MF C11 H14 N2 O6

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s 13 sss full
FULL SEARCH INITIATED 12:33:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 411 TO ITERATE

100.0% PROCESSED 411 ITERATIONS 70 ANSWERS
SEARCH TIME: 00.00.01

L5 70 SEA SSS FUL L3

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 185.88 187.20

FILE 'HCAPLUS' ENTERED AT 12:33:09 ON 12 JUN 2009
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FILE COVERS 1907 - 12 Jun 2009 VOL 150 ISS 25
FILE LAST UPDATED: 11 Jun 2009 (20090611/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 15/thu
      40 L5
      1134118 THU/RL
L6      16 L5/THU
      (L5 (L) THU/RL)

=> s HIV or (human immunodeficiency virus) or AIDS or K65R or M184V or T215Y
      85205 HIV
      2200854 HUMAN
      86717 IMMUNODEFICIENCY
      413899 VIRUS
      65720 HUMAN IMMUNODEFICIENCY VIRUS
      (HUMAN(W) IMMUNODEFICIENCY(W)VIRUS)
      79817 AIDS
      194 K65R
      407 M184V
      178 T215Y
L7      137840 HIV OR (HUMAN IMMUNODEFICIENCY VIRUS) OR AIDS OR K65R OR M184V
      OR T215Y

=> s 16 and 17
L8      14 L6 AND L7

=> d 18 1-14 ti abs bib hitstr

L8      ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI      5'-O-Aliphatic and amino acid ester prodrugs of
      (-)- $\beta$ -D-(2R,4R)-dioxolane-thymine (DOT): Synthesis, anti- HIV
      activity, cytotoxicity and stability studies
AB      A series of (-)- $\beta$ -D-(2R,4R)-dioxolane-thymine-5'-O-aliphatic acid esters
      as well as amino acid esters were synthesized as prodrugs of
      (-)- $\beta$ -D-(2R,4R)-dioxolane-thymine (DOT). The compds. were evaluated
      for anti-HIV activity against HIV-1LAI in human
      peripheral blood mononuclear (PBM) cells as well as for their cytotoxicity
      in PBM, CEM and Vero cells. Improved anti-HIV potency in vitro
```

was observed for the compound 2-4 (5'-O-aliphatic acid esters) without increase in cytotoxicity in comparison to the parent drug. Chemical and enzymic hydrolysis of the prodrugs was also studied, in which the prodrugs exhibited good chemical stability with the half-lives from 3 h to 54 h at pH 2.0 and 7.4 phosphate buffer. However, the prodrugs were relatively labile to porcine esterase with the half-lives from 12.3 to 48.0 min.

AN 2009:137274 HCAPLUS <<LOGINID:20090612>>

DN 150:389124

TI 5'-O-Aliphatic and amino acid ester prodrugs of (-)- β -D-(2R,4R)-dioxolane-thymine (DOT): Synthesis, anti- HIV activity, cytotoxicity and stability studies

AU Liang, Yuzeng; Sharon, Ashoke; Grier, Jason P.; Rapp, Kimberly L.;

Schinazi, Raymond F.; Chu, Chung K.

CS Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA

SO Bioorganic & Medicinal Chemistry (2009), 17(3), 1404-1409

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier B.V.

DT Journal

LA English

IT 1138242-23-5P 1138242-24-6P 1138242-25-7P

1138242-26-8P 1138242-27-9P 1138242-28-0P

1138242-29-1P 1138242-30-4P 1138242-31-5P

1138242-32-6P 1138242-33-7P 1138242-34-8P

1138242-35-9P 1138242-36-0P 1138242-37-1P

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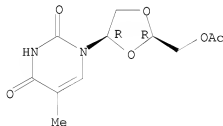
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(aliphatic and amino acid ester prodrugs of D-dioxolane-thymine: preparation, HIV antiviral, cytotoxicity and stability)

RN 1138242-23-5 HCAPLUS

CN 2,4-(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-[(acetyloxy)methyl]-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

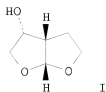
Absolute stereochemistry.



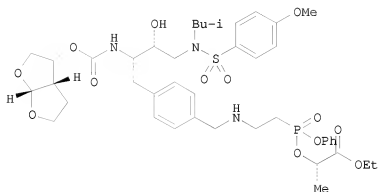
L8 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection

GI



I



II

AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation. The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

AN 2007:1275513 HCAPLUS <<LOGINID::20090612>>

DN 147:502340

TI Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection

IN Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez, Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu

PA Gilead Sciences, Inc., USA

SO PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DT Patent

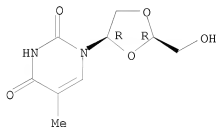
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	WO 2007126812	A2	20071108	WO 2007-US7564	20070329		
	WO 2007126812	A3	20071221				
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA					
	AU 2007245194	A1	20071108			EA 2007-245194	20070329

CA 2647316 A1 20071108 CA 2007-2647316 20070329
 US 20080004242 A1 20080103 US 2007-729522 20070329
 EP 1999133 A2 20081210 EP 2007-754134 20070329
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR
 IN 2008DN07951 A 20081121 IN 2008-DN7951 20080922
 MX 2008012398 A 20081217 MX 2008-12398 20080926
 NO 2008004547 A 20081222 NO 2008-4547 20081028
 KR 2008108322 A 20081212 KR 2008-726569 20081029
 CN 101448838 A 20090603 CN 2007-80017888 20081117
 PRAI US 2006-787126P P 20060329
 WO 2007-US7564 W 20070329
 OS CASREACT 147:502340
 IT 136982-89-3
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (codrug; preparation of carbamic acid bisfuranyl ester compds. as
 HIV protease inhibitors useful in treatment and prevention of
 retroviral infection)
 RN 136982-89-3 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-
 yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Methods and kits for antiviral nucleoside combination dosing for treatment
 of viral infections
 AB The invention is directed to methods and pharmaceutical kits for dosing a
 patient with antiviral nucleosides in an alternating manner.
 AN 2007:966648 HCAPLUS <<LOGINID:20090612>>
 DN 147:292175
 TI Methods and kits for antiviral nucleoside combination dosing for treatment
 of viral infections
 IN Erickson-Viitanen, Susan; Levy, Richard Steven
 PA Pharmasset, Inc., USA
 SO PCT Int. Appl., 98pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007097991	A2	20070830	WO 2007-US4003	20070215
	WO 2007097991	A3	20080612		
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KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
 MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
 RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
 TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AF, EA, EF, OA

PRAI US 2006-773997P P 20060216

OS MARPAT 147:292175

IT 136982-89-3 136982-89-3D, salts or prodrugs

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

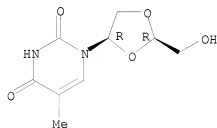
(Biological study); USES (Uses)

(kits; methods and kits for antiviral nucleoside combination dosing for
 treatment of viral infections)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-
 yl]-5-methyl- (CA INDEX NAME)

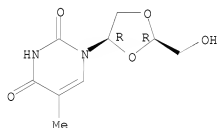
Absolute stereochemistry. Rotation (-).



RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-
 yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Methods for improving the pharmacokinetics of HIV integrase
 inhibitors by administering food and/or ritonavir

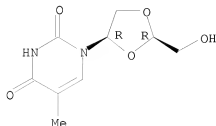
AB The invention provides methods for improving the pharmacokinetics of an
 HIV integrase inhibiting compound by administering food and/or
 ritonavir or a pharmaceutically acceptable salt thereof with the
 HIV integrase inhibitor. Agents and methods are provided that are
 useful for increasing the bioavailability or absorption of integrase

inhibitors, i.e., 4-oxoquinoline compds., such as 6-(3-chloro-2-fluorobenzyl)-1-((2S)-1-hydroxy-3-methylbutan-2-yl)-7-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (I) in order to increase their therapeutic effect in a patient. Thus, coadministration of I (100 mg twice daily) with ritonavir (100 mg twice daily) resulted in a net inhibition of I metabolism and significantly increased systemic exposures; thus, the data supported the use of low-dose ritonavir as a pharmacokinetic booster of I. Concurrent oral administration of I and ritonavir for up to 10 days was generally well-tolerated by patients, all adverse events were mild and transient.

AN 2007:760574 HCAPLUS <<LOGINID:20090612>>
 DN 147:150815
 TI Methods for improving the pharmacokinetics of HIV integrase inhibitors by administering food and/or ritonavir
 IN Kearney, Brian P.; Kakae, Atsuyuki; Kawaguchi, Isao
 PA Gilead Sciences, Inc., USA; Japan Tobacco, Inc.
 SO PCT Int. Appl., 75pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007079260	A1	20070712	WO 2006-US49668	20061229
	WO 2007079260	A9	20070830		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
	AU 2006332664	A1	20070712	AU 2006-332664	20061229
	CA 2635468	A1	20070712	CA 2006-2635468	20061229
	US 20070219243	A1	20070920	US 2006-647858	20061229
	EP 1976517	A1	20081008	EP 2006-848393	20061229
	R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS			
	IN 2008DN05576	A	20080926	IN 2008-DN5576	20080626
	MX 2008008494	A	20080715	MX 2008-8494	20080627
	KR 2008081358	A	20080909	KR 2008-718651	20080729
	NO 2008003333	A	20080929	NO 2008-3333	20080729
	CN 101336107	A	20081231	CN 2006-80052014	20080729
FRAI	US 2005-755039P	P	20051230		
	US 2006-756631P	P	20060106		
	US 2006-763901P	P	20060201		
	WO 2006-US49668	W	20061229		
OS	MARPAT 147:150815				
IT	136982-89-3				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(improving pharmacokinetics of HIV integrase inhibitors by administering food and/or ritonavir)				
RN	136982-89-3 HCAPLUS				
CN	2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)				

Absolute stereochemistry. Rotation (-).

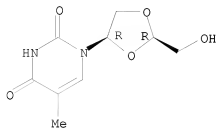


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Pharmacokinetics of the anti-human immunodeficiency
virus agent 1-(β -D-Dioxolane)thymine in rhesus monkeys
AB β -D-Dioxolane-thymine (D-DOT) has potent and selective in vitro
activity against several clin. important resistant human
immunodeficiency virus (HIV) mutants and is in
advanced preclin. development. Therefore, the single-dose i.v. and oral
pharmacokinetics of D-DOT were studied with three rhesus monkeys. The
pharmacokinetic profiles of D-DOT in serum and urine were adequately
described by a two-compartment open pharmacokinetic model. D-DOT was
rapidly and almost completely absorbed (absorption rate constant = 2.7 h⁻¹;
fraction of oral dose absorbed = 0.82 to 1.06). The average serum beta
half-life was 2.16 h. The average central and steady-state vols. of
distributions were 0.52 and 1.02 L/kg of body weight, resp., and the average
systemic and renal clearance values were 0.36 L/h/kg and 0.18 L/h/kg.
Four or eight percent of administered D-DOT was eliminated in the urine as
glucuronide within 8 h after i.v. or oral administration, resp. D-DOT
reached levels in the cerebrospinal fluid in excess of 10 to 20 times the
median effective concentration for wild-type HIV and resistant mutants.
The potent antiretroviral activity of D-DOT against a lamivudine- and
zidovudine-resistant HIV-1 mutant, together with an excellent
pharmacokinetic profile for rhesus monkeys, suggest that further
development is warranted.
AN 2007:741992 HCAPLUS <<LOGINID::20090612>>
DN 147:291288
TI Pharmacokinetics of the anti-human immunodeficiency
virus agent 1-(β -D-Dioxolane)thymine in rhesus monkeys
AU Asif, Ghazia; Hurwitz, Selwyn J.; Obikhod, Aleksandr; Delinsky, David;
Narayanasamy, Janarthanan; Chu, Chung K.; McClure, Harold M.; Schinazi,
Raymond F.
CS Department of Pediatrics, Emory University School of Medicine, Atlanta,
GA, USA
SO Antimicrobial Agents and Chemotherapy (2007), 51(7), 2424-2429
CODEN: AMACQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
IT 136982-89-3
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(pharmacokinetics of D-DOT in rhesus monkeys)
RN 136982-89-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-

yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent

AB (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine (DOT) is a thymidine analog that has potent in vitro activity against wild-type and nucleoside reverse transcriptase inhibitor (NRTI)-resistant HIV. For nucleoside analogs to inhibit viral replication, they must be metabolized to the active triphosphate, which inhibits the viral reverse transcriptase (RT). Using purified enzymes, the kinetics of DOT phosphorylation, inhibition of wild-type and drug-resistant HIV -1 reverse transcriptase activity, and excision of DOT-5'-monophosphate (DOT-MP) from a chain-terminated primer were examined DOT was phosphorylated by human thymidine kinase-1 (TK-1) but not by other pyrimidine nucleoside kinases, including the mitochondrial thymidine kinase (TK-2). Resistance to NRTIs involves decreased binding/incorporation and/or increased excision of the chain-terminating NRTI. RTs containing the D67N/K70R/T215Y/K219Q or T695-SS/T215Y mutations show enhanced removal of DOT-MP from terminated primer as well as approx. four-fold decreased binding/incorporation. The Q151M and K65R mutations appear to cause decreased inhibition by DOT-TP. However, both the K65R and Q151M mutations show decreased excision, which would confer greater stability on the terminated primer. These opposing mechanisms could offset the overall resistance profile and susceptibility. Little or no resistance was observed with the enzymes harboring mutations resistant to lamivudine (M184V) and non-nucleoside RT inhibitors (K103N).

AN 2007:739016 HCAPLUS <<LOGINID:20090612>>
DN 147:268350

TI Mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent

AU Murakami, Eisuke; Bao, Haiying; Basavapathruni, Aravind; Bailey, Christopher M.; Du, Jinfa; Micolochick Steuer, Holly M.; Niu, Congrong; Whitaker, Tony; Anderson, Karen S.; Otto, Michael J.; Furman, Phillip A.

CS Pharmasset Inc., Princeton, NJ, USA

SO Antiviral Chemistry & Chemotherapy (2007), 18(2), 83-92

CODEN: ACCHEH; ISSN: 0956-3202

PB International Medical Press, Ltd.

DT Journal

LA English

IT 136982-89-3

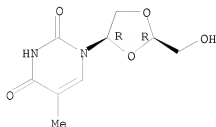
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanism of action of (-)-(2R,4R)-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)thymine as an anti-HIV agent)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)- β -D-(2R, 4R)-dioxolanethymine (DOT) and their anti- HIV activity

AB The synthesis, characterization, anti-HIV activity and cytotoxicity of dendrimers of (-)- β -D-(2R,4R)-dioxolane-thymine (DOT) and polyethylene glycol (PEG)-DOT conjugates are described. Dendrimers in this study were polyamidoamine (PAMAM) generation 2.0, 3.0, 5.0 and 6.0, along with 8.0-branched PEG with a mol. weight of 40 kDa. DOT was attached to PAMAM dendrimers or branched PEG via ester or phosphafte groups. Size exclusion chromatog. was used to purify the dendrimers and PEG conjugates, which were characterized by NMR and MALDI-TOF mass spectrometry. The synthesized PAMAM dendrimers and PEG conjugates were evaluated for anti-HIV activity against HIV-1LAI in primary human peripheral blood mononuclear cells (PBMCs) and cytotoxicity in PBMCs, CEM and Vero cells. PAMAM dendrimers of DOT with ester linkages and particularly phosphate linkers showed an increase in anti-HIV potency in comparison with DOT alone (140- and 56-fold, resp.). Unfortunately, the PAMAM dendrimers also exhibited increased cytotoxicity. Anti-HIV activity of PEG-DOT conjugates was found to be lower than that of DOT.

AN 2007:66477 HCAPLUS <<LOGINID::20090612>>

DN 146:350576

TI PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)- β -D-(2R, 4R)-dioxolanethymine (DOT) and their anti- HIV activity

AU Liang, Yuzeng; Narayanasamy, Janarthanan; Rapp, Kim L.; Schinazi, Raymond F.; Chu, Chung K.

CS The University of Georgia College of Pharmacy, Athens, GA, USA

SO Antiviral Chemistry & Chemotherapy (2006), 17(6), 321-329

CODEN: ACCHEH; ISSN: 0956-3202

PB International Medical Press, Ltd.

DT Journal

LA English

OS CASREACT 146:350576

IT 136982-89-3DP, ethoxylated PAMAM conjugate derivs.

929705-97-5DP, ethoxylated PAMAM conjugate derivs.

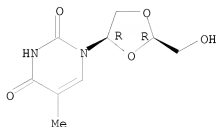
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN

(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti-HIV activity)

RN 136982-89-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

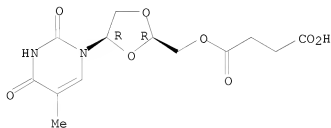
Absolute stereochemistry. Rotation (-).



RN 929705-97-5 HCAPLUS

CN Butanedioic acid, 1-[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] ester (CA INDEX NAME)

Absolute stereochemistry.

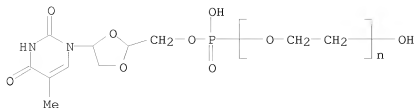


IT 929706-00-3P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (PAMAM dendrimers and branched polyethyleneglycol (nanoparticles) prodrugs of (-)-β-D-(2R, 4R)-dioxolanethymine (DOT) and their anti-HIV activity)

RN 929706-00-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methoxy]hydroxyphosphinyl]-ω-hydroxy- (CA INDEX NAME)



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Phosphoramidate and phosphate prodrugs of
(-)-β-D-(2R,4R)-dioxolane-thymine: Synthesis, anti- HIV
activity and stability studies

AB A series of phosphoramidate and phosphate prodrugs of DOT were synthesized via dichlorophosphate or H-phosphonate chemical and evaluated for their anti-HIV activity against LAI M184V mutants in PBM cells as well as for their cytotoxicity. The antiviral and cytotoxic profiles of the prodrugs were compared with that of the parent compound (DOT), and it was found that four aryl phosphoramidates showed a significant enhancement (8- to 12-fold) in anti-HIV activity without cytotoxicity. Chemical stability of these prodrugs was evaluated in phosphate buffer at pH values of biol. relevance (i.e., pH 2.0 and 7.4). Enzymic hydrolysis was also studied in esterase or lipase in buffer solution. Chemical stability studies indicate that the phosphoramidates have good chemical stability at pH 2.0 and at pH 7.4 phosphate buffer. Phosphoramidate prodrugs were hydrolyzed in vitro by esterase or lipase and found to be better substrates for lipases than for esterases. 1,3-Diol cyclic phosphates showed potent anti-HIV activity without increasing the cytotoxicity compared with that of DOT and have good chemical and enzymic stability. Long-chain lipid phosphates, although showed potent anti-HIV activity, exhibited increased cytotoxicity.

AN 2006:156931 HCAPLUS <<LOGINID::20090612>>

DN 144:403761

TI Phosphoramidate and phosphate prodrugs of
(-)-β-D-(2R,4R)-dioxolane-thymine: Synthesis, anti- HIV
activity and stability studies

AU Liang, Yuzeng; Narayanasamy, Janarthanan; Schinazi, Raymond F.; Chu, Chung K.

CS College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA

SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2178-2189

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier B.V.

DT Journal

LA English

OS CASREACT 144:403761

IT 883989-33-1P 883989-34-2P

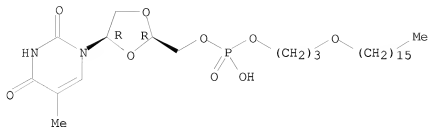
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(phosphoramidate and phosphate prodrugs of
(-)-β-D-(2R,4R)-dioxolane-thymine and synthesis, anti- HIV
activity and stability studies)

RN 883989-33-1 HCAPLUS

CN Phosphoric acid, mono[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] mono[3-(hexadecyloxy)propyl] ester
(CA INDEX NAME)

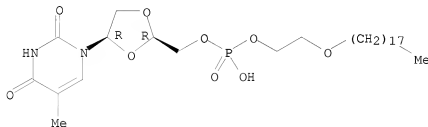
Absolute stereochemistry.



RN 883989-34-2 HCAPLUS

CN Phosphoric acid, mono[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] mono[2-(octadecyloxy)ethyl] ester (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Anti-HIV Activity of (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against Drug-Resistant HIV-1 Mutants and Studies of Its Molecular Mechanism

AB (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine (DOT) is the first thymidine kinase-activated nucleoside that is significantly active against all of the clin. significant NRTI-resistant HIV-1 mutants, including AZT (D67N/K70R/T215Y/K219Q), Tenofovir (K65R), and Lamivudine (M184V). To understand the mol. mechanism of drug resistance and the antiviral activity of DOT against drug-resistant RTs, mol. modeling studies of DOT-TP complexed with the wild-type (WT) and mutated RT were conducted. The key reason for this interesting antiviral activity profile is the presence of a dioxolane ring.

AN 2005:421890 HCAPLUS <<LOGINID:20090612>>

DN 143:90249

TI Anti-HIV Activity of (-)-(2R,4R)-1-(2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against Drug-Resistant HIV-1 Mutants and Studies of Its Molecular Mechanism

AU Chu, Chung K.; Yadav, Vikas; Chong, Youhoon H.; Schinazi, Raymond F.

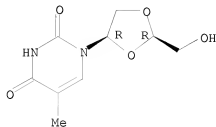
CS College of Pharmacy, University of Georgia, Athens, GA, 30602, USA

SO Journal of Medicinal Chemistry (2005), 48(12), 3949-3952
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

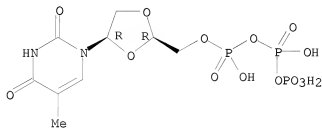
DT Journal
 LA English
 IT 136982-89-3 855138-64-6
 RL: PAC (Pharmacological activity); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (anti-HIV activity of (-)-(2R,4R)-1-
 (2-Hydroxymethyl-1,3-dioxolan-4-yl)thymine against drug-resistant
 HIV-1 mutants and studies of its mol. mechanism)
 RN 136982-89-3 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



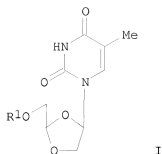
RN 855138-64-6 HCAPLUS
 CN Triphosphoric acid, P-[[(2R,4R)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-1,3-dioxolan-2-yl]methyl] ester (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Dioxolane thymine and combinations for use against 3TC/AZT resistant
 strains of HIV
 GI



AB The present invention relates to the use of a dioxolane thymine compound according to the chemical structure of Formula (I): where R1 is H, an acyl group, a C1-C20 alkyl or ether group, a phosphate, diphosphate, triphosphate or phosphodiester group, for use in the treatment of HIV infections which exhibit resistance to 3TC and/or AZT. Preferably, compds. according to the present invention are combined with at least one anti-HIV agent which inhibits HIV by a mechanism other than through the inhibition of thymidine kinase (TK). These agents include those selected from among nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors, among others. These agents are generally selected from the group consisting of 3TC (Lamivudine), AZT (Zidovudine), (-)-FTC, ddi (Didanosine), ddC (zalcitabine), abacavir (ABC), tenofovir (PMPA), D-D4FC (Reverset), D4T (Stavudine), Racivir, L-D4FC, NVP (Nevirapine), DLV (Delavirdine), EFV (Efavirenz), SQVM (Saquinavir mesylate), RTV (Ritonavir), IDV (Indinavir), SQV (Saquinavir), NFV (Nelfinavir), APV (Amprenavir), LPV (Lopinavir), fuseon and mixts. thereof. The TK dependent agents, such as AZT and D4T, may be used in combination with one of the dioxolane thymine compds. according to the present invention, but the use of such agents may be less preferred. In preferred compns. according to the present invention, R1 is preferably H or a C2-C18 acyl group or a monophosphate group. Pharmaceutical compns. and methods of reducing the likelihood that a patient at risk for contract an HIV infection will contract the infection are other aspects of the present invention.

AN 2004:513490 HCAPLUS <<LOGINID::20090612>>

DN 141:65057

TI Dioxolane thymine and combinations for use against 3TC/AZT resistant strains of HIV

IN Chu, Chung K.; Schinazi, Raymond F.

PA The University of Georgia Research Foundation, Inc., USA; Emory University

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004052296	A2	20040624	WO 2003-US39029	20031208
	WO 2004052296	A3	20040923		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2502625	A1	20040624	CA 2003-2502625	20031208
AU 2003296360	A1	20040630	AU 2003-296360	20031208
EP 1569659	A2	20050907	EP 2003-812874	20031208

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

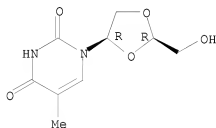
BR 2003017113	A	20051025	BR 2003-17113	20031208
CN 1723025	A	20060118	CN 2003-80105479	20031208
US 20050209196	A1	20050922	US 2005-530088	20050401
MX 2005003637	A	20050816	MX 2005-3637	20050405
IN 2005KN00698	A	20060224	IN 2005-KN698	20050421

PRAI US 2002-431812P P 20021209
 WO 2003-US39029 W 20031208

OS MARPAT 141:65057
 IT 136982-89-3 136982-89-3D, derivs.
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (dioxolane thymine and combinations for use against 3TC/AZT resistant
 strains of HIV)

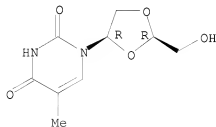
RN 136982-89-3 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-
 yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 136982-89-3 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-
 yl]-5-methyl- (CA INDEX NAME)

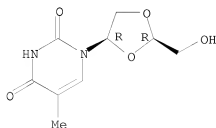
Absolute stereochemistry. Rotation (-).



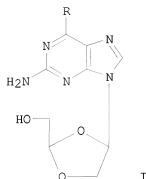
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Molecular mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV
 AB The mutation and resultant adaptability of HIV-1 reverse transcriptase (RT) present a major challenge to the design of the effective antiviral strategies because many initially potent drugs lose efficacy over time. Even though there is an urgent need for a comprehensive understanding of the mol. mechanism of anti-HIV drug resistance by mutant RTs, the unavailability of the structural information of the mutant RTs has prevented detailed investigations. In this study, the active site of the 3TC-resistant (M184V) RT is constructed by a computational method, which clearly shows that the side chain of Val184 occupies the binding site for the nucleoside triphosphates. Therefore, the distance between the side chain of Val184 and the sugar moiety of the nucleoside triphosphate must be closely related to the cross-resistance by M184V RT. The natural substrates, 2'-deoxyribo nucleoside triphosphates, escape from the steric stress from the bulky side chain of Val184 by virtue of the d-sugar conformation as well as the interaction of its 3'-OH group with Tyr115, which locates the nucleoside triphosphate out of the clashing distance from Val184. Similarly, the energy-minimized structures of various d-dioxolane nucleoside triphosphates (TP)/RT complexes indicate that the d-dioxolane sugar moiety acquires enough distance from Val184 due to the specific interaction of its 3'-oxygen atom with the nearby enzyme residues such as Tyr115 and Arg72.
 AN 2004:489072 HCAPLUS <<LOGINID:20090612>>
 DN 141:218359
 TI Molecular mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV
 AU Chong, Youhoon; Chu, Chung K.
 CS Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA, 30602, USA
 SO Antiviral Research (2004), 63(1), 7-13
 CODEN: ARSRDR; ISSN: 0166-3542
 PB Elsevier Science B.V.
 DT Journal
 LA English
 IT 136982-89-3
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (mol. mechanism of dioxolane nucleosides against 3TC resistant M184V mutant HIV)
 RN 136982-89-3 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Preparation of enantiomerically pure β -D-dioxolane nucleosides as
 virucides
 GI



AB A method and composition for the treatment of humans infected with HIV that includes the administration of an HIV treatment amount of an enantiomerically pure β -D-dioxolanyl purine nucleosides I wherein R is OH, Cl, NH₂, or H, or a pharmaceutically acceptable salt or derivative of the compound, optionally in a pharmaceutically acceptable carrier or diluent. Thus, I (R = OH) was prepared and tested in human peripheral blood mononuclear cells for its antiviral activity (EC₅₀ = 0.03 μ M). The toxicity of the compds. were evaluated in uninfected human PBM cells and showed no toxicity at a concentration of 100 μ M.

AN 1999:450894 HCAPLUS <<LOGINID:20090612>>

DN 131:88137

TI Preparation of enantiomerically pure β -D-dioxolane nucleosides as virucides

IN Chu, Chung K.

PA Emory University, USA

SO U.S., 15 pp.

CODEN: USXXAM

DT Patent

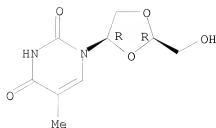
LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5925643	A	19990720	US 1992-935515	19920825
	US 5179104	A	19930112	US 1990-622762	19901205
	CA 2590125	A1	19920625	CA 1991-2590125	19911205
	EP 1164133	A2	20011219	EP 2001-203571	19911205
	EP 1164133	A3	20020102		
	EP 1164133	B1	20070801		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	EP 1600448	A2	20051130	EP 2005-75365	19911205
	EP 1600448	A3	20060823		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	EP 1693373	A1	20060823	EP 2005-77620	19911205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	AT 368660	T	20070815	AT 2001-203571	19911205
	ES 2291268	T3	20080301	ES 2001-203571	19911205

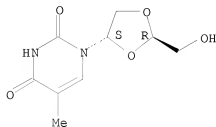
US 5444063	A	19950822	US 1992-967460	19921028
WO 9404154	A1	19940303	WO 1993-US8044	19930825
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9350933	A	19940315	AU 1993-50933	19930825
AU 670637	B2	19960725		
EP 656778	A1	19950614	EP 1993-920366	19930825
EP 656778	B1	20010530		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 93501086	T	19960206	JP 1994-506616	19930825
JP 3519736	B2	20040419		
EP 1081148	A2	20010307	EP 2000-203932	19930825
EP 1081148	A3	20030305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, RO				
ES 2157929	T3	20010901	ES 1993-920366	19930825
JP 2002114787	A	20020416	JP 2001-251947	19930825
CA 2143107	C	20041123	CA 1993-2143107	19930825
US 5684010	A	19971104	US 1995-471533	19950606
US 5767122	A	19980616	US 1995-469465	19950606
AU 9716640	A	19970717	AU 1997-16640	19970327
AU 714646	B2	20000106		
US 5830898	A	19981103	US 1997-838072	19970415
US 5834474	A	19981110	US 1997-839713	19970415
JP 2001097973	A	20010410	JP 2000-246125	20000815
JP 3881165	B2	20070214		
GR 3036393	T3	20011130	GR 2001-401249	20010814
AU 2003200421	A1	20030410	AU 2003-200421	20030207
AU 2003200421	B2	20040408		
JP 2004149543	A	20040527	JP 2003-414876	20031212
JP 2007008959	A	20070118	JP 2006-263009	20060927
PRAI US 1990-622762	A2	19901205		
CA 1991-2099589	A3	19911205		
EP 1992-902800	A3	19911205		
EP 2001-203571	A3	19911205		
JP 1992-502956	A3	19911205		
US 1992-935515	A2	19920825		
US 1992-967460	A3	19921028		
AU 1993-50933	A3	19930825		
EP 1993-920366	A3	19930825		
JP 1994-506616	A3	19930825		
WO 1993-US8044	W	19930825		
US 1995-471533	A3	19950606		
JP 2000-246125	A3	20000815		
OS MARPAT 131:88137				
IT 136982-89-3P 136982-90-6P				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
(preparation of enantiomerically pure dioxolane nucleosides as virucides)				
RN 136982-89-3	HCAPLUS			
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl-	(CA INDEX NAME)			

Absolute stereochemistry. Rotation (-).



RN 136982-90-6 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Preparation of antiviral 1,3-dioxolane nucleoside analogs
 AB This invention includes the compds. 2'-deoxy-5-fluoro-3'-oxacytidines and pharmaceutically acceptable salts thereof for use in medical therapy, for example for the treatment or prophylaxis of an HIV infection (EC50 = 0.013-0.027 μ M) with cytotoxicity of (IC50 < 1 μ M).
 AN 1999:17124 HCAPLUS <<LOGINID::20090612>>
 DN 130:66736
 TI Preparation of antiviral 1,3-dioxolane nucleoside analogs
 IN Liotta, Dennis C.; Schinazi, Raymond F.; Choi, Woo-baeg
 PA Emory University, USA
 SO U.S., 16 pp., Cont.-in-part of U.S. 5,210,085.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 7

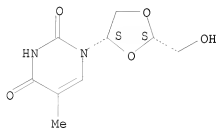
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5852027	A	19981222	US 1993-150012	19931109
	US 5210085	A	19930511	US 1991-659760	19910222
	US 5276151	A	19940104	US 1991-803028	19911206
	WO 9214729	A1	19920903	WO 1992-US1393	19920221
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	AU 715577	B3	20000203	AU 1999-59571	19991119
	AU 2002300661	A1	20030220	AU 2002-300661	20020820
	AU 2002300661	B2	20060608		
PRAI	US 1991-659760	A2	19910222		

US 1991-736089 B2 19910726
 US 1991-803028 A2 19911206
 WO 1992-US1393 W 19920221
 US 1990-473318 A2 19900201
 US 1993-15992 A 19930210
 AU 1999-44745 A3 19990826

IT 127658-07-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of antiviral dioxolane nucleoside analogs)

RN 127658-07-5 HCAPLUS
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl-, rel- (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2009 ACS on STN
 TI Synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs
 AB The present invention relates to a method of preparing the antiviral compds. 2'-deoxy-5-fluoro-3'-thiacytidine (FTC) and various prodrug analogs of FTC from inexpensive precursors with the option of introducing functionality as needed; methods of using these compds., particularly in the prevention and treatment of AIDS; and the compds. themselves. This synthetic route allows the stereoselective preparation of the biol. active isomer of these compds. and related compds. Thus, 2'-deoxy-5-fluoro-3'-thiacytidine was prepared and showed anti-HIV activity (EC50 = 0.011 μ M) and cytotoxicity (IC50 > 100 μ M) in human PBM cells.
 AN 1998:15591 HCAPLUS <<LOGINID::20090612>>
 DN 128:75640
 OREF 128:14803a,14806a
 TI Synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs
 IN Liotta, Dennis C.; Schinazi, Raymond F.; Choi, Woo-bae
 PA Emory University, USA
 SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 402,730.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5700937	A	19971223	US 1995-481556	19950607
	US 5204466	A	19930420	US 1990-473318	19900201

CA	2481078	A1	19910808	CA	1991-2481078	19910131
EP	872237	A1	19981021	EP	1998-201737	19910131
EP	872237	B1	20070117			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP	2001019690	A	20010123	JP	2000-160358	19910131
JP	2002012591	A	20020115	JP	2001-151618	19910131
JP	3530150	B2	20040524			
EP	1772151	A2	20070411	EP	2006-77328	19910131
EP	1772151	A3	20070613			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
US	5210085	A	19930511	US	1991-659760	19910222
US	6703396	B1	20040309	US	1995-402730	19950313
US	5914400	A	19990622	US	1995-472345	19950607
US	6153751	A	20001128	US	1999-337910	19990622
AU	9944745	A	19991111	AU	1999-44745	19990826
AU	715577	B3	20000203	AU	1999-59571	19991119
JP	2001352997	A	20011225	JP	2001-151617	20010521
JP	3844978	B2	20061115			
AU	2002300661	A1	20030220	AU	2002-300661	20020820
AU	2002300661	B2	20060608			
JP	2005053893	A	20050303	JP	2004-146115	20040517
JP	4108645	B2	20080625			
JP	2006141408	A	20060608	JP	2006-33782	20060210
AU	2006207874	A1	20060928	AU	2006-207874	20060907
PRAI	US 1990-473318	A2	19900201			
	US 1991-659760	A2	19910222			
	US 1991-736089	B1	19910726			
	US 1993-92248	B1	19930715			
	US 1995-402730	A2	19950313			
	AU 1991-73004	A3	19910131			
	CA 1991-2075189	A3	19910131			
	EP 1991-904454	A3	19910131			
	EP 1998-201737	A3	19910131			
	JP 1991-504897	A3	19910131			
	GB 1991-4741	A	19910306			
	GB 1991-9505	A	19910502			
	US 1993-15992	A1	19930210			
	US 1994-215498	B1	19940321			
	US 1995-472345	A1	19950607			
	AU 1999-44745	A3	19990826			
	JP 2001-151617	A3	20010521			
	AU 2002-300661	A3	20020820			
IT	127658-07-5P					
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)					
	(synthesis and antiviral activity of 2'-deoxy-5-fluoro-3'-thiacytidine and nucleoside analogs)					
RN	127658-07-5 HCAPLUS					
CN	2,4(1H,3H)-Pyrimidinedione, 1-[(2R,4R)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-5-methyl-, rel- (CA INDEX NAME)					

Relative stereochemistry.